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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/883,119	06/14/2001	Andrew D. Ellington	TEXAS-11147	8203

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EXAMINER	
EPPS FORD, JANET L	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
11/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/883,119	ELLINGTON ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9-14,128,138 and 139* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9-14,128,138 and 139* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Sequence Listing Compliance

2. Applicant's sequence submission on 7-12-07 was entered.

Response to Arguments

Claim Rejections - 35 USC § 112

3. Claims 1-5, 9-14, and 128 remain rejected and claim 138 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Written Description.

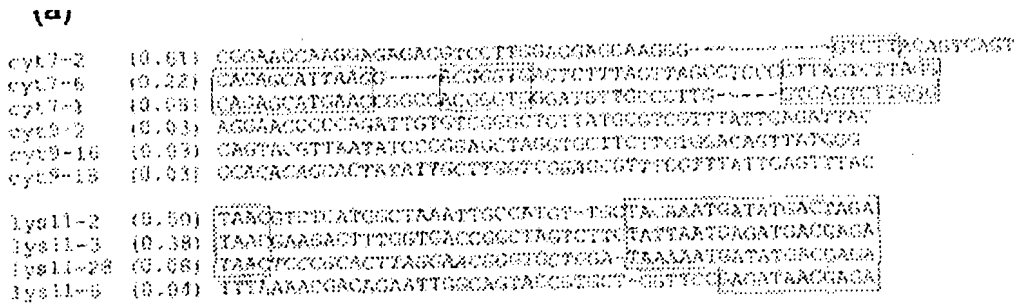
4. Applicant's arguments filed 7/11/07 have been fully considered but they are only partially persuasive.

(1) Applicant's submission of the sequence listing 7/11/07 removes the grounds for rejection over the insertion of SEQ ID NO: 67 into the claims, as set forth in the prior Office Action.

(2) Applicants traversed the instant rejection on the grounds that the specification as filed discloses at least 5 specific and working examples of a peptide effector, thus Applicants argue that this disclosure is sufficient to meet the intent of 35 USC 112, 1st paragraph. Contrary to Applicant's assertions, Applicant's disclosure of the following

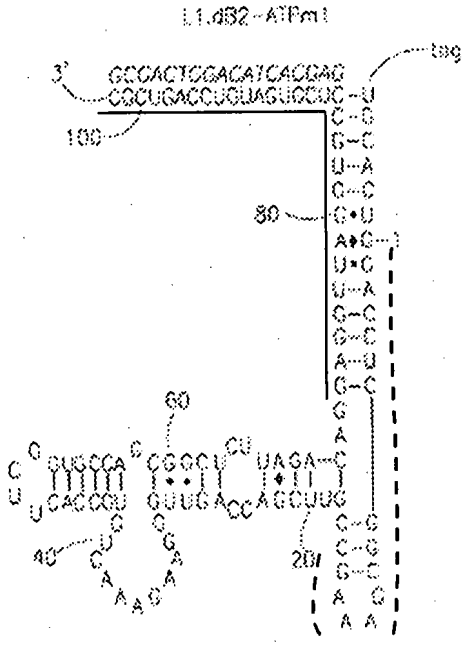
nucleotide sequences that correspond to the N50 region of the peptide regulatable catalytic polynucleotides of the instant invention is not sufficient to describe the full scope of polynucleotides that are regulated by a peptide effector as encompassed by the instant claims.

The specification as filed at Figure 19(a) discloses the following structures, which correspond to the N50 nucleotide structures that are regulated by peptide effectors:



However, it is noted that the instant claims are not limited to any particular peptide effector, and the number polynucleotide structures encompassed by the N50 region of the instant claims, comprises 4^{50} or 1.27×10^{30}. Applicant's disclosure of the above sequences is not sufficient to state that Applicants were in possession of the full scope of sequences encompassed by the instant claims, wherein a peptide effector regulates the polynucleotide. Although the claims recites some structural portions of the claimed polynucleotides, these sequences do not define sequences that are known in the art to be regulated by a peptide effector as required by the claims. The defined regions of the polynucleotides according to SEQ ID NO: 67 of the instant claims are known in the art to be associated with an RNA ligase that is regulated by ATP, see for example the following structure (Figure 5c of Nathan et al.), wherein the underlined sequences of

SEQ ID NO: 67, correspond to the sequences of the ATP RNA ligase: Ggaccucggcgaaagc-N50-gagguuaggugccucgugauguccagucgc:



There is no correlation between the 50 undefined nucleotides encompassed by the polynucleotide sequence forth in the instant claims, and its catalytic activity, wherein said catalytic activity is ligation, and wherein this activity is regulated by an undefined peptide effector. Moreover, it is noted that the term "regulated" encompasses both enhancement and suppression. The structure of these random nucleotides must be identified empirically by further experimentation. According to Knight et al. (2003), the "[s]election of novel activities from randomized sequence pools of 10^{12}–10^{15} unique nucleic acid molecules (~2–2000 pmol), is remarkably successful at finding new nucleic acid ligands and catalysts. However, even the 10^{15} molecules in a large experiment cover only a tiny fraction of the possible sequences, e.g. a random region of just 20 nt

has 4^{20} or 1.1×10^{12} possible sequences, and a random region of 100 has 4^{100} or 1.6×10^{60} possible sequences. Consequently, although the initial sequences recovered from SELEX are highly optimized, they frequently *are not the best possible solutions*." In the instant case, we are looking at a potential $1.27 \text{ X } 10^{30}$ sequences that are potentially regulated by an undefined peptide effector, and Applicant's disclosure does not set forth a sufficient number of species to indicate that they were in possession of the full scope of the claimed invention as of the filing date of the instant application.

As stated in the prior Office Action, as per MPEP § 2163, "[A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between *that function and the structure of the sequence*, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." However, the catalytic core used in the method is randomized within the catalytic core region. The structures of each individual catalytic core that is regulated by a peptide effector encompassed by the claimed genus, must be identified empirically. Thus, based upon this observation it is immediately apparent that applicants were not in possession of the full scope of peptide effectors encompassed by the instantly claimed invention.

Claim Rejections - 35 USC § 103

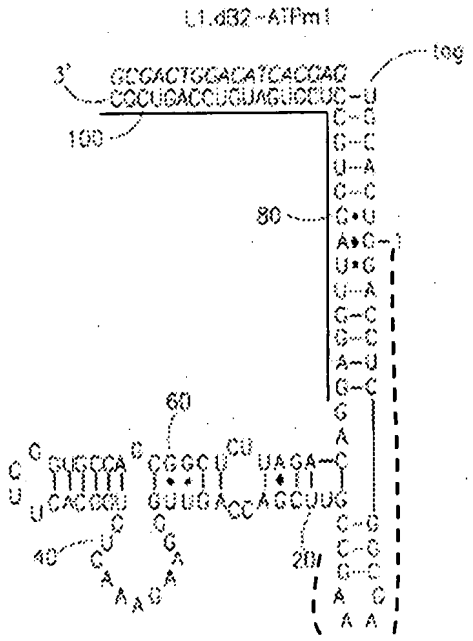
5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-5, 9-14, 128, and 138-139 are rejected under 35 U.S.C. 103(a) as being obvious over Nathan et al. (WO 2000/24931 A2; 5/04/2000).

The instant claims recite a polynucleotide comprising the sequence 5' GGACCUCGGCGAAAGC-N50-GAGGUU-AGGUGCCUCGUGAUGUCCAGUCGC3' (SEQ ID NO: 67), where N is any nucleotide.

The defined regions of the polynucleotides according to SEQ ID NO: 67 of the instant claims are known in the art to be associated with an RNA ligase that is regulated by ATP, see for example the following structure (Figure 5c of Nathan et al.), wherein the underlined sequences of SEQ ID NO: 67, correspond to the sequences of the ATP RNA ligase: SEQ ID NO: 67: Ggaccucggcgaaagc-N50-gagguuaggugccucgugauguccagucgc:



The RNA ligase of Nathan et al. differs from the polynucleotide of the instant claim to the extent that there are 56 residues in the "N" region instead of the 50 recited in the

instant claims. This 56 base pair portion is a non-conserved region of the L1 ribozyme, which is not required for the catalytic activity of Ligation. Moreover, this reference also teaches that new allosteric ribozymes can be formed by swapping the non-conserved region of ribozymes with aptamers that are capable of binding proteins (see pages 18-19, bridging paragraph). Additionally, the methods of Nathan et al. comprises wherein the examples of non-nucleic acid analytes (i.e. which potentially function to allosterically regulate the ribozymes) include proteins, peptides, glycoproteins, glycopeptidnes, membranal fragments, phosphorylated nucleotides, hormones, drugs, organic or non-organic, etc. (see bridging paragraph of pages 3-4).

It would have been obvious to the ordinary skilled artisan seeking alternative allosterically modified ribozymes to modify the non-conserved region of the L1 ribozyme ligase of Nathan et al. with an aptameric region that binds a peptide. One of skill in the art would have been motivated to make this modification since Nathan clearly demonstrates that this region can be modified allosterically modified with an aptamer, wherein binding of an exogenous compound to said aptamer results in the regulation of the L1 ligase catalytic activity. Moreover, absent evidence to the contrary, the peptide or protein effector recited in the claims, and the number of nucleotides separating the conserved regions appears to be a difference in design choice since the disclosure of Nathan et al. teaches that a randomized sequence of 90 base pairs can be used to select for alternative allosterically regulated ribozyme structures (see Figure 1A), however in the modified L1 ribozyme set forth in Figure 5A is only 56 base pairs in length. Additionally, because the methods of Nathan et al. comprise wherein the

examples of non-nucleic acid analytes (i.e. which potentially function to allosterically regulate the ribozymes) include proteins, peptides, glycoproteins, glycopeptidnes, membranal fragments, phosphorylated nucleotides, hormones, drugs, organic or non-organic, etc. (see bridging paragraph of pages 3-4). Therefore, as stated above, the use of a peptide, protein, phosphorylated protein, etc, is obvious to the extent that it is merely a design choice based upon the disclosure of Nathan et al.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE